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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/555,349	08/01/00	TEDDER T	180/95/PCT/U

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EXAMINER	
LI,Q	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 07/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/555,349	Applicant(s) TEDDER, THOMAS F.	
	Examiner Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *14-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 August 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election of Group I without traverse in Paper No. 10 is acknowledged. Claims 14-28 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Claims 1-13 are under current examination.

Specification

The disclosure is objected to because of the following informalities:

The specification contains nucleic acid and amino acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth as follows: The paper copy and the CRF is not identical. This is because the paper copy is in the old format and the CRF is in the new format. Applicant must resolve the contradiction in sequence listing by providing a substitute paper copy of the Sequence Listing and a new statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office action must include a complete response to the requirement for a new Sequence Listing.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 recites "the animal having antibody-producing cells with a manipulated characteristic that facilitates the antibody-producing cell's ability to produce antibodies". Claim 8 recites "the animal having antibody-producing cells with disrupted peripheral tolerance". Given the broadest reasonable interpretation, the claims embrace a broad class of cells having a manipulated characteristic promoting antibody production, or with disrupted peripheral tolerance.

In view of the guidance provided in the specification, the specification defines "disrupted peripheral tolerance" as "any manipulation or alteration of the peripheral tolerance of the antibody-producing cells". The specification provides teachings that CD19 transgenic mice having disrupted peripheral tolerance, and would produce autoantibodies. The specification discusses some molecules in the CD19-CD21 complex regulatory pathway that influence antibody production, such as CD22, and C3. However, the specification does not provide an adequate disclosure to all molecules that would alter antibody production, and all possible methods of cellular manipulation.

For example, *Strasser et al* teach transgenic mice harboring human Bcl-2 cDNA under the control of an immunoglobulin heavy chain enhancer. The transgenic mice have a great excess of B lymphocytes, Ig-secreting cells and serum immunoglobulins. Immunization of these mice would lead to an amplified and protracted antibody response. (See abstract and result section, Proc Natl Acad Sci USA 1991;88:8661-65). *Yoshino et al* teach immunizing an animal with the anti-IL-4 antibody would enhance IgG2a antibody production to hen egg lysozyme (Eur J Pharmacol 1997 Oct;336:203-9).

In analyzing whether the written description requirement is met for the claimed subject matter as a genus of cells having recited characteristics, a representative number of species has to be disclosed by their complete sequences, structure, and other relevant identifying characteristics, such as biological functions. The genus encompasses any cell that producing antibodies, not possible in unmanipulated controls or in an increased quantity and/or facilitated process compared with unmanipulated controls, thus encompassing an uncountable number of possible cells. Considering the potential methods of manipulation that would be encompassed by the claims, the disclosed CD19-CD21 pathway is not a representative species of the genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of *any* and *all* cells having a manipulated characteristic or a disrupted peripheral tolerance. Therefore, only the described CD19 transgene manipulation meets the written description provision of 35 U.S.C. §112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 7, 8, and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7, 8, and 13 are vague and indefinite because the claim recitation "high affinity". The specification does not define the term, and fails to provide a standard for ascertaining the requisite degree of the high affinity, and one of the skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6-10, 12, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by *Hammerling et al.*

These claims are drawn to a method for production of a monoclonal antibody to an antigen comprising the step of immunizing an animal having manipulated antibody-producing cells, preferably B lymphocytes, wherein said manipulation leads to disrupted peripheral tolerance, and facilitates antibody production, wherein the steps further comprise removing said cells from said animal, forming and propagating a hybridoma, and harvesting the monoclonal antibodies produced, wherein the animal is a mouse.

Hammerling et al teach a method for production of monoclonal antibodies having narrow specificity for polymorphic HLA alloantigens, comprising the step of immunizing a HLA-transgenic mice line having self-tolerance (a disrupted peripheral tolerance) to a particular HLA molecule, with skin grafts and lymphoid cells (antigen) of a second HLA-transgenic mouse expressing a different HLA molecule, such that a specific immune response to a particular allelic HLA difference between donor and recipient transgenic mice is elicited. *Hammerling et al* teach further removing the spleen cells of the immunized mice with high serum antibody titers, fusing with myeloma cells, propagating hybridomas, harvesting and characterizing the produced monoclonal antibodies. The

method taught by *Hammerling et al* facilitates specific anti-HLA alloantigen monoclonal antibody production, thus, *Hammerling et al* anticipate the instant claims.

Claims 1, 3, 4, 6, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by *WO9614401.*

These claims are drawn to a method for production of a monoclonal antibody to an antigen comprising the step of immunizing an animal having manipulated antibody-producing cells, preferably B lymphocytes, wherein said manipulation facilitates antibody production, wherein the steps further comprise removing said cells from said animal, forming and propagating a hybridoma, and harvesting the monoclonal antibodies produced.

WO9614401 teach a method for monoclonal antibody production comprising the step of immunizing a transgenic animal with an antigen, wherein the lymphocytes of the transgenic animal contain genetic material, which confers a selectable phenotype thereon (a manipulated characteristic), the method steps further comprise removing the lymphocytes from said animal, fusing the manipulated lymphocytes with immortal cells to produce hybridomas, selectively culturing the hybridomas, and harvesting the monoclonal antibodies produced (claims 17,18, and pages 21-22 of the specification). The specification goes on to teach that the selectable phenotype could be a HPRT, and because the selectable marker in the lymphocyte of the transgenic animal obviates the requirement for a HPRT selection process and expands the repertoire of fusion partner

cells that can be used in hybridoma formation, the manipulation facilitates monoclonal antibody production. Thus, WO9614401 anticipates the instant claims.

No claim is allowed. Claims 5 and 11 are free of cited prior art of record, because the cited prior art of record fails to teach using a CD19 transgenic mouse line to facilitate monoclonal antibody production. However, these claims are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen M Hauda can be reached on 703-305-6608. The fax numbers for the organization where this application or proceeding is assigned are 703-308-8724 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Kay Pinsky, whose telephone number is (703) 305-3553.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
July 13, 2001

ROBERT A. SCHWARTZMAN
PRIMARY EXAMINER